

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1-116 were originally filed.

The preliminary amendment to the claims received on August 10, 2006 canceled claims 2-18, 20, 22-24, 26-33, 35-37, 39-40, 43, 45, 47-48, 51-102, 104-108, 111-113, and 115 and amended claims 21, 25, 46, 109, and 114.

The amendment to the claims received on March 28, 2011 canceled claims 1, 38, 41, 42, 44, and 116; amended claims 19, 21, 25, 34, 46, 49, 50, 103, 109, 110, and 114; and added new claims 117-144.

The amendment to the claims received on September 2, 2011 amended claims 19, 25, 114, 120, 121, 127, 129, 130, 131, 132, 143, and 144 and added new claim 145.

Claims 19, 21, 25, 34, 46, 49, 50, 103, 109, 110, 114, and 177-145 are currently pending.

Claims 19, 21, 25, 34, 117-127, 129, and 145 are currently under consideration.

### ***Election/Restrictions***

Applicants elected, without traverse, Group II in the reply filed on March 28, 2011. Upon further consideration, the restriction between Groups I, II, and III is withdrawn (i.e. all methods of isolating cell/cells are considered a single invention). In addition, it is respectfully noted that any attempts by applicant or applicants' representative to alter the final outcome of the elected method (i.e. isolation of cell or cells), present new claims with different method steps, etc. may result in a restriction requirement or withdrawal of claims via election by original presentation (i.e. see amended claim 130). Claims 46, 49, 103, 109, 110, 114, 133-144 (i.e. drawn to nonelected Group IX); 50 (i.e. drawn to nonelected Group VIII); and 128, 130, 131, and 132 (i.e.

drawn to nonelected Groups IV, V, or X) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

***Priority***

The present application claims status as a 371 (National Stage) of PCT/US05/05080 filed February 17, 2005 which claims the benefit of 60/546,075 filed February 18, 2004.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/546,075, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. provisional application 60/546,075 fails to disclose shRNA. Therefore, any claims referring to shRNA have a priority date of February 17, 2005.

***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on September 2, 2011 is being considered by the examiner.

### **Withdrawn Objections**

The objection to the abstract is withdrawn in view of the amendment received on September 2, 2011.

The objection to the disclosure regarding the first line of the specification is withdrawn in view of the amendment received on September 2, 2011.

The objection to the disclosure regarding embedded hyperlinks and/or other form of browser-executable code is withdrawn in view of the amendment received on September 2, 2011.

### **Withdrawn Rejections**

The rejection of claims 120, 121, and 127 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of the claim amendments received on September 2, 2011.

### **New Rejections Necessitated by Amendment**

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 21, 25, 34, 117-120, 122-127, 129, and 145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection. Support in the originally filed specification was not found for “wherein the plurality comprises two or more subsets of cells”. In addition, applicants neglected to point out support for the present amendment to independent claim 19.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 145 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. How can a cell be isolated when the RNA or protein is lethal?

### **Maintained Rejections**

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 125 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. Present claim 125 is considered an improper use claim. Therefore, it is not clear what method steps are required by the claim. See MPEP § 2173.05(q).

***Arguments and Response***

Applicants' arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claim 125 were considered but are not persuasive for the following reasons.

Applicants contend that the incorporated method steps from claim 19 and the "selecting" step render the claim definite.

Applicants' arguments are not convincing since the "using the selection marker after introducing the DNA into the cells but prior to exposing said cells to the signaling probe" is considered indefinite. Applicants may wish to amend the claim to read "utilizing the selection marker after introducing the DNA into the cells but prior to exposing said cells to the signaling probe" to clarify the claim language.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19, 21, 25, 34, 117-127, 129, and 145 are rejected under 35 U.S.C. 102(a) as being anticipated by Shekdar et al. U.S. Patent 6,692,965 issued February 17, 2004 (filed November 22, 2000; effective filing date November 23, 1999).

For present claims 19, 21, 25, 34, 117-127, 129, and 145, Shekdar et al. teach methods comprising introducing into cells at least one DNA encoding at least one antisense RNA or mRNA (i.e. protein encoding; expression) and at least one epitope tag (i.e. encompassing library, first and second library, etc.), exposing the cells to molecular beacons that hybridize to the antisense RNA, mRNA, and/or nucleic acid encoding the epitope tag(s), isolating cells that fluoresce, and culturing cells to produce cell lines wherein cells can be pooled or mixed wherein the epitope tag can be in frame or out of frame with the DNA encoding the RNA, selection markers can be utilized, promoters are utilized, and the RNA or protein encoded by the RNA can be lethal to the cells (please refer to the entire specification particularly the abstract; columns 1-9, 11, 13-17; Examples; claims). Regarding the functional limitations (i.e. “preselected”, “test”, “same or related biological pathway”, “upstream or downstream of each other”, “modulating, activating, or repressing function to each other”, “dependent on each other for function or activity”, “components of the same complex”, or “same protein family”), applicants are respectfully directed to MPEP § 2173.05(g).

Therefore, the teachings of Shekdar et al. anticipate the presently claimed invention.

***Arguments and Response***

Applicants’ arguments directed to the rejection under 35 USC 102 (a) as being anticipated by Shekdar et al. for claims 19, 21, 25, 34, 117-127, 129, and 145 were considered but are not persuasive for the following reasons.

Applicants contend that Shekdar et al. do not teach the method of present independent claim 19 particularly a method of isolating a plurality of cells encoding a plurality of different RNAs associated with a same nucleic acid tag sequence.

Applicants' arguments are not convincing since the teachings of Shekdar et al. anticipate the method of the instant claims. Shekdar et al. teach methods comprising introducing into cells **at least one** DNA encoding **at least one** antisense RNA or mRNA (i.e. protein encoding; expression) and **at least one** epitope tag (i.e. encompassing library, first and second library, etc.), exposing the cells to molecular beacons that hybridize to the antisense RNA, mRNA, and/or nucleic acid encoding the epitope tag(s), isolating cells that fluoresce, and culturing cells to produce cell lines wherein cells can be pooled or mixed wherein the epitope tag can be in frame or out of frame with the DNA encoding the RNA, selection markers can be utilized, promoters are utilized, and the RNA or protein encoded by the RNA can be lethal to the cells (please refer to the entire specification particularly the abstract; columns 1-9, 11, 13-17; Examples; claims). Thus, Shekdar et al. teach the method of the present claims. In addition, it is respectfully noted that, as presently claimed, each of the plurality of DNAs does not have to encode a different RNA, but only the plurality must encode a plurality of different (e.g. 10 DNAs encoding 5 different RNAs would read on the present claims) and only a subset of DNAs encodes the same nucleic acid tag sequence (e.g. the 6 DNAs encoding the same RNA with the same nucleic acid tag sequence). In addition, Shekdar et al. teach one of the advantages of the disclosed method is utilizing a limited or small number of molecular beacons corresponding to the number of different epitope tags is needed to prepare a large number of different cells and the advantage of the epitope tag detection method is that separate beacons to each antisense RNA do not have to be made (please refer to the entire specification particularly columns 2, 14, 15).

Claims 19, 21, 25, 117-120, 122-127, 129, and 145 are rejected under 35 U.S.C. 102(e) as being anticipated by Short et al. U.S. Patent Application Publication 2003/0215798 published November 20, 2003 (filed June 16, 1997).

For present claims 19, 21, 25, 117-120, 122-127, 129, and 145, Short et al. teach methods of identifying and isolating clones comprising introducing expression libraries into cells and utilizing molecular beacons to detect cells wherein selection markers, promoters, etc. may be utilized (please refer to the entire specification particularly the abstract; paragraphs 50-61, 77, 78, 116, and 121-199).

Therefore, the teachings of Short et al. anticipate the presently claimed invention.

***Arguments and Response***

Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Short et al. for claims 19, 21, 25, 117-120, 122-127, 129, and 145 were considered but are not persuasive for the following reasons.

Applicants contend that Short et al. do not teach the method of present independent claim 19. Applicants contend that Short et al. relates to a fundamentally different invention because Short et al. refers to a high throughput functional screen utilizing FACS® to identify cells in a prokaryotic expression library that possess a biological activity of interest (i.e. enzymatic activity) utilizing enrichment steps with molecular beacons (i.e. Short et al. is sorting for positive clones based on enzymatic activity not on RNA detection as presently claimed).

Applicants' arguments are not convincing since the teachings of Short et al. anticipate the method of the instant claims. Short et al. teach utilizing FACS® for DNA recovery, hybridization to a probe of interest, utilizing labels including complementary homopolymeric oligonucleotides,

and *in vivo* biopanning methods utilizing molecular beacons (please refer to the entire specification particularly paragraphs 17, 33, 85-89, 94-113, and **116**).

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19, 21, 25, 34, 117-127, 129, and 145 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6,692,965. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. Patent 6,692,965 are drawn to methods of generating cells/cell lines via introducing into cells DNA encoding at least one RNA, exposing cells to at least one molecular beacon that hybridizes to the RNA, isolating cells that fluoresce, and growing cells wherein the RNA includes antisense RNA which may be lethal to the cell, utilizing additional epitope tags that can be in frame or out of frame with the DNA encoding the RNA, utilizing conditional promoters, and utilizing drug resistant markers(see claims 1-33).

#### ***Arguments and Response***

Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 6,692,965 for claims 19, 21, 25, 34, 117-127, 129, and 145 were considered but are not persuasive for the following reasons.

Applicants contend that they "stand ready to submit a terminal disclaimer...upon indication of otherwise allowable subject matter".

Applicants' arguments are not convincing since the claimed invention of 6,692,965 renders obvious the method of the instant claims. In addition, while a request may be made that

objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

Claims 19, 21, 25, 34, 117-127, 129, and 145 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 12/771,223. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in 12/771,223 are drawn to methods of generating a cell line via transfecting cells with at least one DNA encoding RNA, exposing cells to molecular beacons that hybridize to RNA, isolating cells that fluoresce, and growing cells wherein drug resistant markers are utilized, antisense RNA is utilized, epitope tags are utilized that can be in frame or out of frame, etc. (see claims 1-43).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### ***Arguments and Response***

Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 12/771,223 for claims 19, 21, 25, 34, 117-127, 129, and 145 were considered but are not persuasive for the following reasons.

Applicants contend that they "stand ready to respond to the rejection or provide a terminal disclaimer, as appropriate, upon allowance of the claims".

Applicants' arguments are not convincing since the claimed invention of 12/771,223 renders obvious the method of the instant claims. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/  
Primary Examiner, Art Unit 1654